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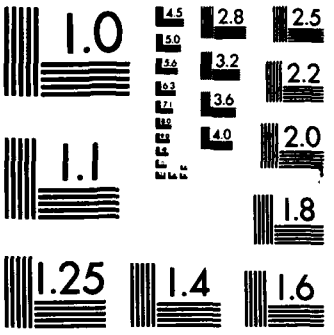


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Arlington, VA 22217

RE: "Large scale neuronal circuits for selective storage and recognition of complex stimuli: A pilot study"
Contract # N00014-85-K-0650

Dear Joel:

Enclosed is our final technical report on the above contract.

Sincerely,

Gary Lynch

Donald M. Perkel

/jsp

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# Large-scale neuronal circuits for selective storage and recognition of complex stimuli: A pilot study.

## Final Report

1 July 1987

We have undertaken studies on the nature and behavior of neural circuits based on the known anatomical and physiological characteristics of cortical circuits in rat brain. We have focused on olfactory (piriform) cortex, for a number of reasons, including the fact that piriform cortex is phylogenetically old, and significantly simpler than neocortical areas, and that piriform receives its inputs monosynaptically from the olfactory bulb, which in turn receives inputs monosynaptically from the nasal epithelium, directly in response to chemical olfactory inputs. This offers an unusual opportunity to study cortical mechanisms operating on inputs that have only minimally been preprocessed, in contrast to the inputs to other cortical areas (even sensory cortical areas) that receive extensive preprocessing before reaching the cortex. Keywords: Nerve transmission

We have constructed a computational model of piriform cortex, based on its known anatomical and physiological characteristics, including sparse connectivity between bulb and layer II; EPSP and IPSP properties including excitatory feedback and long and short feedforward and feedback inhibitory currents; multiple cell firing frequencies; a two-step firing threshold; necessary conditions for LTP induction; cell-specific long afterhyperpolarization (AHP); relative duration of short EPSPs and short and longer IPSPs; and so on. Experimentation with the computer simulation has identified network-level functional properties not immediately apparent from its cellular-level physiology, as well as revealing gaps in the extant physiological data, thereby suggesting experiments to provide answers to the questions thus raised.

Larson and Lynch (1986) found that 'patterned' stimulation of CA1, consisting of short (30ms) bursts at 100Hz, separated by an interburst interval of 200ms (i.e., bursts occuring at $\approx 5Hz$, the theta rhythm), produce optimal synaptic potentiation *in vitro*, without any artificial blocks of inhibition necessary. The same patterned stimulation, applied to the lateral olfactory tract, produces LTP in piriform cortex correlated with behavioral learning in rats performing an olfactory discrimination task (Staubli et al, 1986). An unanswered question is how the transient synaptic facilitation produced by patterned stimulation (the 'priming' effect) interacts with existing potentiation in synapses that have previously been potentiated. In network simulations it frequently occurs that previously-potentiated synapses are activated in a theta burst pattern; formalization of the rule underlying LTP induction requires specification of the function that combines stable potentiated synaptic strength values with the increment due to transient facilitation. Experimental comparisons were made of the net depolarization produced by four-pulse bursts given in the theta pattern on naive vs potentiated synapses. Early results indicate that LTP sums nonlinearly with priming; i.e., previously-potentiated synapses are only slightly more effective in depolarizing tar-

get dendrites than are naive synapses during theta bursting stimulation (Larson et al., unpublished data). Hypothesizing that theta bursting corresponds to learning mode in a behaving animal, these results suggest that synaptic conductance will differ in learning (theta bursting) vs. performance (non-theta burst) firing modes, in marked contrast to typical network models.

A related question is how synaptic change is affected in the presence of asynchronous stimulation of multiple pathways, which undoubtedly occurs *in situ* and in any network model containing feedback. Theoretical considerations in the simulation prompted experiments on these temporal attributes of LTP using staggered bursts arriving on a primed target, such that burst 2 began halfway through burst 1, and burst 3 began halfway through burst 2. Preliminary results show retrograde facilitation, a counterintuitive result in which burst 1 generated strong LTP, while burst 3 generated only slight potentiation, indicating an inverse relation between arrival time and magnitude of induced synaptic potentiation.

Implementation of certain of these features into a computer simulation of the superficial layers of the piriform (olfactory) cortex have provided some insight into the consequences of these properties of LTP induction to the behavior of brain networks. In particular, upon exposure to a large array of input vectors with varying degrees of similarity, cells in the model begin to generate two types of output signals: one associated with a cue's unique identity (i.e., orthogonalization of cues), and the other associated with the similarity of a cue to other learned cues (i.e., clustering of cues). Thus, learning rules based on empirically-derived LTP induction rules appear to facilitate the development of hierarchical levels of representation within cortical circuitries.

These and related results have indicated that computer simulations of real brain structures can be of value not only for interpretation of existing experimental results, but also for specification of further experiments. Our simulations have led to a series of experiments that have given rise to counterintuitive findings, with the dual benefit of advancing the body of data on the physiological mechanisms underlying LTP, and further constraining the set of biologically-valid models of cortical networks, enabling us to move closer to an understanding of the nature of such networks.

## PUBLICATIONS

Roman, F., Staubli, U. and Lynch, G. Evidence for synaptic potentiation in a cortical network during learning. Brain Research, in press.

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